REMARKS

Claims 24, 30, 31 and 37 are pending in this application.

I. Claim Rejections Under 35 U.S.C. § 103

The Examiner rejects claims 24 and 30 under 35 U.S.C. § 103(a) as being unpatentable over Segers et al. (US 5,383,324), Veech (US 4,663,166), Nakamura et al. (US 6,867,193), Panter-Brick (Europ. J. Intensive Care Medicine) and Kido et al. (US 6,129,925). Applicants respectfully traverse the rejection.

A. Limitations of Claim 24

An aseptic combination preparation of claim 24 is characterized by the following limitations:

(i) a first solution containing dipotassium hydrogen phosphate, glucose, sodium chloride, sodium lactate, calcium gluconate, magnesium sulfate and zinc sulfate in a first chamber;

(ii) a second solution containing dipotassium hydrogen phosphate and at least one amino acid selected from the group consisting of L-leucine, L-isoleucine, L-valine, L-lysine hydrochloride, L-threonine, L-tryptophan, L-methionine, L-phenylalanine, L-cysteine, L-tyrosine, L-arginine, L-histidine, L-alanine, L-proline, L-serine, glycine, L-aspartic acid and L-glutamic acid in a second chamber; and

(iii) the first solution and the second solution each have a potassium ion concentration of about 13 to 35 mEq/L.

B. Problem to be solved by invention of Claim 24

When an infusion preparation in which a medicinal ingredient containing a potassium ion as an electrolyte at a high concentration is accommodated in one chamber of a plurality of chambers, routine mistakes can result in the administration of only the medicinal ingredient (potassium ion of high concentration) to the patient. When the potassium ion concentration is excessively high, such patient may develop hyperkalemia and, in the worst case, the patient may die by cardiac arrest (see, page 3, lines 20 to 29 of the specification).

Claim 24 relates to an aseptic combination preparation which solves this problem, as disclosed on page 4, lines 15 to 18 of the specification.

Segers, Veech, Nakamura, Panter-Brick and Kido neither teach nor suggest the above-

mentioned problem and therefore would not be combined to reach the claimed invention.

Concretely, (1) Segers teaches devices and methods for stabilizing bicarbonate solutions (column 3, SUMMARY OF THE INVENTION, lines 33 to 34);

(2) Veech teaches electrolyte solutions which are useful in electrolyte and fluid therapy, parenteral nutrition, and dialysis (abstract, lines 1 to 3);

(3) Nakamura teaches an amino acid preparation for preventing onset of hepatic encephalopathy caused by conventional amino acid preparations and enhancing amelioration of the symptoms (column 2, lines 1 to 4);

(4) Panter-Brick teaches intravenous nutrition with a metabolic mineral mixture containing calcium lactate, dipotassium hydrogen phosphate, disodium hydrogen phosphate, magnesium sulfate, calcium chloride, zinc sulfate, etc. (page 47, table 5); and

(5) Kido teaches an infusion preparation set (a container filled with infusion liquids) useful for preparation of an infusion liquid containing sugars, amino acids, electrolytes, a fat emulsion and vitamins (abstract, lines 1 to 5).

Therefore, the problem to be solved by invention of claim 24 is not obvious over the cited references.

C. Comparison of limitations among Claim 24 and the cited references

a) Segers

Segers discloses that "In a preferred embodiment, the upper chamber 44 can further include sodium chloride, potassium chloride, dextrose and dextrose polymers (column **7,** lines 37 to 39)".

However, Segers neither discloses nor suggests limitation (i) a first solution containing dipotassium hydrogen phosphate(emphasis added), glucose, sodium chloride, sodium lactate, calcium gluconate, magnesium sulfate and zinc sulfate in a first chamber as recited in claim 24.

Segers discloses that "Likewise, the lower chamber 46 can further include sodium chloride, potassium chloride, amino acids, peptides and glycerol (column **7,** lines 39 to 41)".

However, Segers does not disclose or suggest limitation (ii) a second solution containing dipotassium hydrogen phosphate (emphasis added) and at least one amino acid selected from the group consisting of L-leucine, L-isoleucine, L-valine, L-lysine hydrochloride, L-threonine, L-tryptophan, L-methionine, L-phenylalanine, L-cysteine, L-tyrosine, L-arginine, L-histidine, L-

alanine, L-proline, L-serine, glycine, L-aspartic acid and L-glutamic acid in a second chamber as recited in claim 24.

Segers discloses that "when the solution contained in the upper chamber 44 is mixed with the solution contained in the lower chamber 46, the subsequent peritoneal dialysis solution has the following composition; --- 0 to about 3.0 (mmol/L) potassium (emphasis added) (column 7, lines 42-50)". That is, Segers discloses only the concentration of potassium ion after mixing the solutions.

However, Segers neither discloses nor suggests the first solution and the second solution having a potassium ion concentration of about 13 to 35 mEq/L (emphasis added) of limitation (iii) of claim 24. In addition, there is neither motivation nor clue for those skilled in the art to adopt the claimed potassium ion concentration of about 13 to 35 mEq/L before mixing the first solution and the second solution. Further, the claimed potassium concentration range of about 13 to 35 mEq/L is far from the range of 0.0 to about 3.0 mmol/L of Segers and potassium is contained as not an essential component but an optional component.

Therefore, those skilled in the art would not have arrived at the invention of claim 24 from Segers.

b) Veech

Veech discloses that potassium ion is 0 to about 90 mEq/L on column 35, Table III.

However, Veech neither discloses nor suggests the first solution containing the specific combination of dipotassium hydrogen phosphate and glucose and the like and the second solution containing the specific combination of dipotassium hydrogen phosphate and amino acid and the like as recited in limitations (i) and (ii) of claim 24.

Thus, Veech is silent about limitations (i) and (ii) of claim 24.

Further, Veech neither discloses nor suggests that the first solution and the second solution each have a potassium ion concentration of about 13 to 35 mEq/L of limitation (iii) of Claim 24. In Veech, potassium ion concentration of 0 to about 90 mEq/L is not a concentration in each chamber but a concentration at the time of administration. Thus, there is neither motivation nor clue for those skilled in the art to adopt the claimed potassium ion concentration of about 13 to 35 mEq/L before mixing the first solution and the second solution. Further, potassium ion is contained as not an essential component but an optional component in Veech's solution.

Therefore, those skilled in the art would not have arrived at the invention of claim 24 from Veech.

c) Nakamura

Nakamura neither discloses nor suggests a potassium ion concentration itself in the first solution and the second solution.

That is, Nakamura is silent about limitation (iii) of claim 24, as well as limitations (i) and (ii) as dipotassium hydrogen phosphate is contained in the first solution and the second solution.

Further, in Nakamura, there is neither motivation nor clue for those skilled in the art to adopt the claimed potassium ion concentration of about 13 to 35 mEq/L before mixing the first solution and the second solution.

Therefore, those skilled in the art would not have arrived at the invention of claim 24 from Nakamura.

d) Panter-Brick

Panter-Brick discloses intravenous nutrition with a metabolic mineral mixture containing calcium lactate, dipotassium hydrogen phosphate, disodium hydrogen phosphate, magnesium sulfate, calcium chloride, zinc sulfate etc (page 47, table 5) .

However, Panter-Brick neither discloses nor suggests use of dipotassium hydrogen phosphate and the concentration of potassium ion before mixing the first solution and the second solution.

Thus, Panter-Brick neither discloses nor suggests limitations (i) to (iii) of claim 24.

Further, in Panter-Brick, there is neither motivation nor clue for those skilled in the art to adopt the claimed potassium ion concentration of about 13 to 35 mEq/L before mixing the first solution and the second solution.

Thus, those skilled in the art would not have arrived at the invention of claim 24 from Panter-Brick.

e) Kido

Kido discloses an infusion preparation set useful for preparation of an infusion liquid containing sugar, amino acids, electrolytes, a fat emulsion and vitamins (abstract, lines 1 to 4).

However, Kido neither discloses nor suggest use of dipotassium hydrogen phosphate and the concentration of potassium ion before mixing the first solution and the second solution.

Thus, Kido neither discloses nor suggests limitations (i) to (iii) of claim 24.

Further, in Kido, there is neither motivation nor clue for those skilled in the art to adopt the claimed potassium ion concentration of about 13 to 35 mEq/L before mixing the first solution and the second solution.

Thus, those skilled in the art would not have arrived at the invention of claim 24 from Kido.

f) Conclusion

In order to arrive at the invention of claim 24, it is necessary to arrive at not only containing at least dipotassium hydrogen phosphate in the first solution and the second solution but also adjusting the concentration of potassium ion before mixing the first solution and the second solution containing dipotassium hydrogen phosphate.

For the foregoing reasons, those skilled in the art would not have arrived at limitation (iii) of claim 24, as well as the specific combination of limitation (iii) with limitations (i) and (ii) of claim 24, from Segers, Veech, Nakamura, Panter-Brick and Kido.

D. Unexpected effects of the invention of Claim 24

In the aseptic combination preparation of claim 24, the potassium ion concentration of each medical solution to be accommodated in a plurality of chambers is adjusted in a proper range, and there is no risk of causing hyperkalemia, etc. As a result, the preparation of claim 24 can prevent adverse effects due to medical errors if the medicinal solution in only one chamber is administered to a patient by mistake (page 6, lines 6 to 15 of the specification).

Thus, claim 24 exhibits the remarkably effect of preventing adverse effects, such as hyperkalemia and cardiac arrest caused by medical error.

Segers, Veech, Nakamura, Panter-Brick, and Kido neither teach nor suggest the remarkably effect of the invention of claim 24.

For example:

(l) the purpose of Segers is to stabilize bicarbonate solutions (column 3, lines 33 to 34);

(2) the purpose of Veech is to normalize the Na:Cl ratio, plasma and cellular pH and cellular cofactor ratio, in a manner which decreases toxicity over prior art solutions (abstract, lines 3 to 6);

(3) the purpose of Nakamura is to prevent onset of hepatic encephalopathy caused by conventional amino preparations, and to enhance the amelioration of the symptoms (column 2, lines 1 to 4);

(4) the purpose of Panter-Brick is to provide intravenous nutrition being a practical and safe form of therapy for minimizing weight loss in newborns who cannot feed by mouth (abstract, lines 4 to 5); and

(5) the purpose of Kido is to be highly stable without suffering from precipitation, phase separation, denaturation and similar problems (column 16, lines 6 to 8).

The purpose and effects disclosed in Segers, Veech, Nakamura, Panter-Brick and Kido are quite different from the effect of eliminating adverse effects caused by a medical mistake.

Therefore, the remarkable effect of claim 24 would not have been expected from Segers, Veech, Nakamura, Panter-Brick and Kido.

Accordingly, claim 24 is not obvious over the cited references.

Therefore, claim 24 would not have been obvious over the references.

Claim 30 depends from claim 24, and thus also would not have been obvious over the references.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

The Examiner rejects claims 31 and 37 under 35 U.S.C. § 103(a) as being unpatentable over Segers et al., Nakamura et al., Kido et al. and Stone et al. (US 4,489,0.97). Applicants respectfully traverse the rejection.

A. Limitations of Claim 31

An aseptic combination preparation of claim 31 is characterized by the following limitations:

(iv) a first solution containing sodium chloride, glucose, calcium chloride and magnesium chloride in a first chamber;

(v) a second solution containing sodium chloride, sodium hydrogen carbonate, potassium dihydrogen phosphate and potassium chloride in a second chamber; and

(vi) the first solution and the second solution each have an osmotic pressure ratio of about 1 relative to physiological saline.

B. Problem to be solved by invention of Claim 31

When the osmotic pressure ratio of a medicinal ingredient-containing solution divided and accommodated in one chamber of a plurality of chambers is excessively high or low, and when the chambers are not communicated so that the medical ingredients are properly mixed,

only the medicinal ingredient solution is administered to a patient. This causes severe vessel pain and destruction of erythrocytes in the blood (page 3, last line to page 4, lines 8 to 18 of the specification).

Claim 31 provides an aseptic combination preparation which solves this problem, as disclosed on page 4, lines 15 to 18 of the specification.

Segers, Nakamura, Kido and Stone neither teach nor suggest the above-mentioned problem.

For example, (1) Segers teaches devices and methods for stabilizing bicarbonate solutions (column 3, SUMMARY OF THE INVENTION, lines 33 to 34);

(2) Veech teaches electrolyte solutions which are useful in electrolyte and fluid therapy, parenteral nutrition, and dialysis (abstract, lines 1 to 3);

(3) Nakamura teaches an amino acid preparation for preventing onset of hepatic encephalopathy caused by conventional amino acid preparations and enhancing amelioration of the symptoms (column 2, lines 1 to 4);

(4) Kido teaches an infusion preparation set (a container filled with infusion liquids) useful for preparation of an infusion liquid containing sugars, amino acids, electrolytes, a fat emulsion and vitamins (abstract, lines 1 to 5); and

(5) Stone teaches that antifugal/antibacterial materials are added to sterile compositions intended for administration to humans or lower animals to minimize bacterial and mycotic contamination which can cause infections associated with the medical and veterinary use of such compositions (abstract, lines 1 to 5).

Therefore, the problem to be solved by invention of claim 31 is not obvious over the cited references.

C. Comparison of limitations among Claim 31 and the cited references

a) Segers

Segers discloses that "In a preferred embodiment, the upper chamber 44 can further include sodium chloride, potassium chloride, dextrose and dextrose polymers (column 7, lines 37 to 39)".

However, Segers neither discloses nor suggests limitation (iv) a first solution containing sodium chloride, glucose, calcium chloride and magnesium chloride in a first chamber as recited in claim 31.

Segers discloses that "Likewise, the lower chamber 46 can further include sodium chloride, potassium chloride, amino acids, peptides and glycerol (column 7, lines 39 to 41)".

However, Segers does not disclose or suggest sodium chloride, sodium hydrogen carbonate, potassium dihydrogen phosphate and potassium chloride or the specific combination thereof in a second solution in a second chamber.

Thus Segers neither discloses nor suggests limitation (v) as recited in claim 31.

Segers neither discloses nor suggests that the first solution and the second solution each have an osmotic pressure ratio of about 1 relative to physiological saline (emphasis added) of limitation (vi) of claim 31. In Segers, there is neither motivation nor clue for those skilled in the art to adopt the osmotic pressure ratio of about 1 relative to physiological saline before mixing the first solution and the second solution.

Therefore, those skilled in the art would not have arrived at limitations (iv) to (vi) of claim 31 from Segers.

b) Nakamura

Nakamura discloses electrolytes such as sodium, potassium, calcium, chloride, sugar and the like (column 4, lines 4 to 10).

However, Nakamura neither discloses nor suggests limitations (iv) and (v) of claim 31.

Nakamura discloses that the drug solution after sterilization had an osmotic pressure ratio of 2.8 to 3.3 (column 5, lines 12 to 14).

That is, Nakamura's solution teaches an osmotic pressure ratio after mixing the solution(s).

Thus, the cited reference neither discloses nor suggests that the first solution and the second solution each have an osmotic pressure ration of about 1 relative to physiological saline (emphasis added) of limitation (vi) of claim 31.

Further, one of ordinary skill in the art would have had no reason or motivation to prepare an aseptic combination preparation with an osmotic pressure ratio of about 1 relative to physiological saline before mixing the first solution and the second solution.

Moreover, the recited osmotic pressure ratio of about 1 before mixing the first solution and the second solution is clearly distinct from an osmotic pressure ratio of 2.8 to 3.3 after mixing the solution(s) such that one of ordinary skill in the art would not expect them to have similar properties.

Thus, those skilled in the art would not have arrived at the invention of claim 31 from Nakamura.

c) Kido

Kido discloses an infusion preparation set useful for preparation of an infusion liquid containing sugar, amino acids, electrolytes, a fat emulsion and vitamins (abstract; column 6, lines 23 to 44).

However, Kido neither discloses nor suggests limitations (iv) and (v) of claim 31.

In addition, Kido neither discloses nor suggests that the first solution and the second solution each have an osmotic pressure ration of about 1 relative to physiological saline (emphasis added) of limitation (vi) of claim 31.

Further, one of ordinary skill in the art would have had no reason or motivation to prepare an aseptic combination preparation with an osmotic pressure ratio of about 1 relative to physiological saline before mixing the first solution and the second solution.

Thus, those skilled in the art would not have arrived at the invention of claim 31 from Kido.

d) Stone

Stone discloses an intravenous electrolyte solution containing potassium dihydrogen phosphate, potassium phosphate, potassium chloride, and other salts and sugar (column 12, example 1, lines 45 to 60).

However, Stone neither discloses nor suggests limitations (iv) and (v) of claim 31.

In addition, Stone neither discloses nor suggests an osmotic pressure ratio itself. That is, Stone neither discloses nor suggests that the first solution and the second solution each have an osmotic pressure ratio of about 1 relative to physiological saline (emphasis added) of limitation (vi) of claim 31. In Stone, there is neither motivation nor clue for those skilled in the art to adopt the claimed osmotic pressure ratio of about 1 relative to physiological saline before mixing the first solution and the second solution.

Thus, one of skilled in the art would not have arrived at an osmotic pressure ratio of about 1 relative to physiological saline of limitation (vi) as well as the combination of limitation (vi) with limitations (iv) and (v) of claim 31 from Stone.

e) Conclusion

In order to arrive at the invention of claim 31, it is necessary to arrive at not only

containing each components in the first solution and the second solution but also adjusting an osmotic pressure ratio before mixing the first solution and the second solution.

For the foregoing reasons, those skilled in the art would not have arrived at limitation (vi) of claim 31, as well as the specific combination of limitation (vi) with limitations (iv) and (v) of claim 31, from Segers, Nakamura, Kido and Stone.

D. Unexpected effect of the invention of Claim 31

In the aseptic combination preparation of Claim 31, the osmotic pressure ratio of each medical solution in each chamber is adjusted in a proper range, and there is no risk of causing hemolysis due to low osmotic pressure, etc. As a result, the preparation of claim 31 prevents adverse effects by medical errors if the medicinal solution in only one chamber is administered to a patient by mistake, as disclosed on page 6, lines 6 to 15 of the specification.

Therefore, the invention of claim 31 exhibits remarkably effects over the cited references.

Segers, Nakamura, Kido and Stone neither teach nor suggest the remarkably effects of claim 31.

The purposes of Segers, Nakamura and Kido are disclosed above.

The purpose of Stone is that antifungal/antibacterial materials are added to sterile compositions intended for administration to humans or lower animals to minimize bacterial and mycotic contamination which can cause infections associated with medical and veterinary uses of such compositions (abstract, lines 1 to 5).

Thus, the purpose and effects of Segers, Nakamura, Kido and Stone are quite different from preventing hemolysis and cardiac arrest.

Therefore, claim 31 would not have been obvious over the references.

Claim 37 depends from claim 31, and thus also would not have been obvious over the references.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

II. Conclusion

For these reasons, Applicants take the position that the presently claimed invention is clearly patentable over the applied references.

Therefore, in view of the foregoing remarks, it is submitted that the rejections set forth by the Examiner have been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Nobuaki SUMIYOSHI et al.

/William R. Schmidt, II/
Digitally signed by /William R. Schmidt, II/
DN: cn=/William R. Schmidt, II/, o, ou, email=bschmidt@wenderoth.com, c=US
Date: 2011.07.21 14:49:00 -04'00'

By _____
William R. Schmidt, II
Registration No. 58,327
for
Andrew B. Freistein
Registration No. 52,917
Attorney for Applicants

WRS/emj
Washington, D.C. 20005-1503
Telephone (202) 721-8200
Facsimile (202) 721-8250
July 21, 2011